

What is claimed is:

1. An antisense compound 8 to 50 nucleobases in length, wherein said compound specifically hybridizes with nucleotides 2920-3420 as set forth in SEQ ID NO:3 and inhibits expression of mRNA encoding human apolipoprotein B after 16 to 24 hours by at least 30% in 80% confluent HepG2 cells in culture at a concentration of 150 nM.
2. The antisense compound of claim 1, wherein said compound specifically hybridizes with nucleotides 3230-3288 as set forth in SEQ ID NO:3 and inhibits expression of mRNA encoding human apolipoprotein B after 16 to 24 hours by at least 30% in 80% confluent HepG2 cells in culture at a concentration of 150 nM.
3. The antisense compound of claim 1 or 2 that is an antisense oligonucleotide.
4. The antisense compound of claim 3, wherein the antisense oligonucleotide is an oligonucleotide mimetic compound.
5. The antisense compound of claim 1 or 2, twelve to thirty nucleobases in length.
6. The antisense compound of claim 5, fourteen to twenty nucleobases in length.
7. The antisense compound of claim 4, wherein the oligonucleotide mimetic compound comprises at least one phosphorothioate linkage.

8. The antisense compound of claim 4, wherein the oligonucleotide mimetic compound comprises at least one 2'-O-methoxyethyl sugar moiety.
9. The antisense compound of claim 4, wherein the oligonucleotide mimetic compound comprises at least one 5-methylcytosine.
10. The antisense compound of claim 1 or 2, wherein the antisense compound is a chimeric antisense compound.
11. The antisense compound of claim 10, wherein the chimeric antisense compound is a chimeric phosphorothioate antisense compound.
12. The antisense compound of claim 11, wherein the chimeric phosphorothioate antisense compound comprises 2'-methoxyethoxyl nucleotide wings and a 2'-deoxynucleotide gap.
13. The antisense compound of claim 12, wherein the chimeric phosphorothioate antisense compound comprises ten 2'-deoxynucleotides.
14. The antisense compound of any one of claims 1-13, wherein said antisense compound inhibits expression of mRNA encoding human apolipoprotein B after 16 to 24 hours by at least 50% in 80% confluent HepG2 cells in culture at a concentration of 150 nM.
15. The antisense compound of any one of claims 1-13, wherein at least one oligonucleotide is covalently linked to a conjugate.

16. A composition comprising the antisense compound of any one of claims 1-13 and a pharmaceutically acceptable carrier or diluent.
17. The composition of claim 16 further comprising a colloidal dispersion system.
18. A composition comprising an antisense compound of any of claims 1-13 hybridized to a complementary strand.
19. The composition of claim 18, wherein the hybridization of the antisense compound to the complementary strand forms at least one blunt end.
20. The composition of claim 19, wherein the hybridization of the antisense compound to the complementary strand forms two blunt ends.
21. An antisense oligonucleotide compound 8 to 50 nucleobases in length comprising at least 8 contiguous nucleotides of SEQ ID NO:247.
22. The antisense oligonucleotide compound of claim 21, wherein the antisense oligonucleotide compound has a sequence comprising SEQ ID NO:247.
23. The antisense oligonucleotide compound of claim 22, twelve to thirty nucleobases in length.
24. The antisense oligonucleotide compound of claim 23, fourteen to twenty nucleobases in length.
25. The antisense oligonucleotide compound of claim 24, wherein the antisense oligonucleotide compound has a sequence consisting of SEQ ID NO:247.

26. The antisense oligonucleotide compound of claim 25, wherein the antisense oligonucleotide compound is an oligonucleotide mimetic compound.
27. The antisense oligonucleotide compound of claim 26, wherein the oligonucleotide mimetic compound is a chimeric phosphorothioate oligonucleotide compound.
28. The antisense oligonucleotide compound of claim 27, wherein the chimeric phosphorothioate oligonucleotide compound comprises 2'-methoxyethoxyl nucleotide wings and a 2'-deoxynucleotide gap.
29. The antisense oligonucleotide compound of claim 28, wherein the chimeric phosphorothioate oligonucleotide compound comprises ten 2'-deoxynucleotides.
30. The oligonucleotide compound of any one of claims 21-29, wherein at least one oligonucleotide is covalently linked to a conjugate.
31. A composition comprising the antisense oligonucleotide compound of any of claims 21-29 and a pharmaceutically acceptable carrier or diluent.
32. The composition of claim 31 further comprising a colloidal dispersion system.
33. A composition comprising an oligonucleotide compound of any of claims 22-29 hybridized to a complementary strand.
34. The composition of claim 33, wherein the hybridization of the oligonucleotide compound to the complementary strand forms at least one blunt end.

35. The composition of claim 34, wherein the hybridization of the oligonucleotide compound to the complementary strand forms two blunt ends.
36. A method of inhibiting the expression of apolipoprotein B in cells or tissues comprising contacting said cells or tissues with a compound of claim 2 under conditions such that expression of apolipoprotein B is inhibited.
37. A method of inhibiting the expression of apolipoprotein B in cells or tissues comprising contacting said cells or tissues with a compound of claim 21 under conditions such that expression of apolipoprotein B is inhibited.
38. The method of claim 36 or claim 37, wherein the cells or tissues are contacted *in vivo*.
39. The method of claim 38, wherein said contacting comprises the step of administering the compound to an animal.
40. The method of claim 39, wherein the animal is a human.
41. The method of claim 40, wherein the human has a disease or condition associated with apolipoprotein B expression and a therapeutically or prophylactically effective amount of the compound is administered.
42. The method of claim 41, wherein the human has a condition associated with abnormal lipid metabolism.

43. The method of claim 41, wherein the human has a condition associated with abnormal cholesterol metabolism.
44. The method of claim 41, wherein the human has a cardiovascular disease.
45. The method of claim 44, wherein the cardiovascular disease is atherosclerosis.
46. The method of claim 41, wherein the human has an abnormal metabolic condition associated with apolipoprotein B expression.
47. The method of claim 46, wherein the abnormal metabolic condition is hyperlipidemia.
48. The method of claim 41, wherein the human has diabetes.
49. The method of claim 41, wherein the human is obese.
50. The method of claim 40, wherein an effective amount of the compound is administered to prevent a disease or condition associated with apolipoprotein B expression.
51. The method of claim 40, wherein an effective amount of the compound is administered to delay a disease or condition associated with apolipoprotein B expression.
52. A method of preventing or delaying the onset of an increase in glucose levels in an animal comprising administering to said animal a therapeutically or prophylactically effective amount of the compound of claim 1.

53. A method of preventing or delaying the onset of an increase in glucose levels in an animal comprising administering to said animal a therapeutically or prophylactically effective amount of the compound of claim 22.
54. The method of claim 52 or claim 53 wherein the animal is a human.
55. The method of claim 54 wherein the glucose levels are serum or plasma glucose levels.
56. A method of modulating serum cholesterol levels in an animal comprising administering to said animal a therapeutically or prophylactically effective amount of the compound of claim 1 or 21.
57. The method of claim 56 wherein the animal is a human.
58. A method of modulating lipoprotein levels in an animal comprising administering to said animal a therapeutically or prophylactically effective amount of the compound of claim 1.
59. A method of modulating lipoprotein levels in an animal comprising administering to said animal a therapeutically or prophylactically effective amount of the compound of claim 22.
60. The method of claim 58 or claim 59 wherein the animal is a human.
61. The method of claim 60 wherein the lipoprotein is VLDL.
62. The method of claim 60 wherein the lipoprotein is HDL.

63. The method of claim 60 wherein the lipoprotein is LDL.
64. The method of any one of claims 39, 52, 53, 56, 58, and 59 wherein the compound is administered intravenously.
65. The method of any one of claims 39, 52, 53, 56, 58, and 59 wherein the compound is administered subcutaneously.
66. An antisense oligonucleotide compound 20 nucleobases in length having a sequence of nucleobases as set forth in SEQ ID NO:247 and comprising 5-methylcytidine at nucleobases 2, 3, 5, 9, 12, 15, 17, 19, and 20, wherein every internucleoside linkage is a phosphothioate linkage, nucleobases 1-5 and 16-20 comprise a 2'-methoxyethoxyl modification, and nucleobases 6-15 are deoxynucleotides.
67. The antisense oligonucleotide compound of claim 66, wherein at least one oligonucleotide is covalently linked to a conjugate.
68. A composition comprising the antisense oligonucleotide compound of claim 66 and a pharmaceutically acceptable carrier or diluent.
69. The composition of claim 68 further comprising a colloidal dispersion system.
70. A composition comprising the antisense oligonucleotide compound of claim 66 hybridized to a complementary strand.



71. A method of inhibiting the expression of apolipoprotein B in cells or tissues comprising contacting said cells or tissues with a compound of claim 66 so that expression of apolipoprotein B is inhibited.
72. The method of claim 71, wherein the cells or tissues are contacted *in vivo*.
73. The method of claim 72, wherein said contacting comprises the step of administering the compound to an animal.
74. The method of claim 73, wherein the animal is a human.
75. The method of claim 74, wherein the human has a disease or condition associated with apolipoprotein B expression and a therapeutically or prophylactically effective amount of the compound is administered.
76. The method of claim 75, wherein the human has a condition associated with abnormal lipid metabolism.
77. The method of claim 75, wherein the human has a condition associated with abnormal cholesterol metabolism.
78. The method of claim 75, wherein the human has a cardiovascular disease.
79. The method of claim 78, wherein the cardiovascular disease is atherosclerosis.
80. The method of claim 75, wherein the human has an abnormal metabolic condition associated with apolipoprotein B expression.

81. The method of claim 80, wherein the abnormal metabolic condition is hyperlipidemia.
82. The method of claim 75, wherein the human has diabetes.
83. The method of claim 75, wherein the human is obese.
84. The method of claim 74, wherein an effective amount of the compound is administered to prevent a disease or condition associated with apolipoprotein B expression.
85. The method of claim 74, wherein an effective amount of the compound is administered to delay a disease or condition associated with apolipoprotein B expression.
86. A method of preventing or delaying the onset of an increase in glucose levels in a human comprising administering to said human a therapeutically or prophylactically effective amount of the compound of claim 66.
87. The method of claim 86 wherein the glucose levels are serum glucose levels.
88. The method of claim 86 wherein the glucose levels are plasma glucose levels.
89. A method of modulating serum cholesterol levels in a human comprising administering to said human a therapeutically or prophylactically effective amount of the compound of claim 66.
90. A method of modulating lipoprotein levels in a human comprising administering to said human a

therapeutically or prophylactically effective amount of the compound of claim 66.

91. The method of claim 90 wherein the lipoprotein is VLDL.
92. The method of claim 90 wherein the lipoprotein is HDL.
93. The method of claim 90 wherein the lipoprotein is LDL.
94. The method of any one of claims 73-93 wherein the compound is administered intravenously.
95. The method of any one of claims 73-93 wherein the compound is administered subcutaneously.
96. The method of any one of claims 39, 52, 53, 56, 58, 59, and 73-93 wherein the compound is administered subcutaneously.
97. A compound comprising a first nucleobase strand hybridized to a second nucleobase strand, each strand 8 to 50 nucleobases in length, said first nucleobase strand comprising a sequence of at least 8 contiguous nucleobases of nucleotides 2920-3420 as set forth in SEQ ID NO:3, said second nucleobase strand comprising a sequence sufficiently complementary to said first strand so as to permit stable hybridization, said compound inhibiting expression of mRNA encoding human apolipoprotein B after 16 to 24 hours by at least 30% in 80% confluent HepG2 cells in culture at a concentration of 100 nM.
98. The compound of claim 97, wherein said first nucleobase strand comprises a sequence of at least 8

contiguous nucleobases of nucleotides 3230-3288 as set forth in SEQ ID NO:3.

99. The compound of claim 98, wherein the first strand comprises a sequence of 12 to 30 contiguous nucleobases of nucleotides 3230-3288 as set forth in SEQ ID NO:3.
100. The compound of claim 98, wherein the first strand comprises a sequence of 20 contiguous nucleobases of nucleotides 3230-3288 as set forth in SEQ ID NO:3.
101. The compound of claims 98, 99, or 100, wherein the second strand comprises a sequence perfectly complimentary to at least 8 contiguous nucleobases of nucleotides 3230-3288 as set forth in SEQ ID NO:3.
102. The compound of claim 101, wherein the second strand comprises a sequence perfectly complimentary to 12 to 30 nucleobases of nucleotides 3230-3288 as set forth in SEQ ID NO:3.
103. The compound of claim 101, wherein the second strand comprises a sequence perfectly complimentary to 20 nucleobases of nucleotides 3230-3288 as set forth in SEQ ID NO:3.
104. The compound of claim 103, wherein at least one strand comprises RNA.
105. The compound of claim 104, wherein at least one strand comprises one or more deoxynucleosides.
106. The compound of claim 98, wherein the hybridized strands form at least one blunt end.

107. The compound of claim 98, wherein the hybridized strands form at least one overhanging end.
108. The compound of claim 107, wherein the overhanging end comprises at least one modified base.